IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Patent Application of

HAYNES et al — Atty. Ref.: 01579-0968

Serial No. 10/518,523 — TC/A.U.: 1648

Filed: August 17, 2005 — Examiner: Humphrey, L.W.Z.

For: IGG FC/HIV-GP120/C3D FUSION PROTEIN

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December 22, 2009

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

APPEAL BRIEF

Sir:

Appellants hereby appeal the final rejection of claims 1-17, in the Office Action dated February 19, 2009, and submit the present Appeal Brief pursuant to 37 CFR § 41.37. A Notice of Appeal was filed July 20, 2009.

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(I) REAL PARTY IN INTEREST

The real party in interest is Duke University, Durham, North Carolina 27708-0083, by way of an Assignment from the inventors to Duke University, Durham, North Carolina 27708-0083, recorded in the U.S. Patent and Trademark Office on August 17, 2005, at Reel 017019, Frame 0086.

(II) RELATED APPEALS AND INTERFERENCES

Appellants, Appellants' legal representative, and the assignee are not aware of any related prior or pending appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in this appeal.

(III) STATUS OF CLAIMS

Claims 1-22 are pending. Claims 1-17 have been finally rejected. Claims 18-22 stand withdrawn from consideration.

Claims 1-17 are the subject of the present appeal. A copy of claims 1-17 is attached as a Claims Appendix, pursuant to Rule 41.37(c)(1)(viii).

(IV) STATUS OF AMENDMENTS

No Amendment Under Rule 116 has been filed in response to the final Office Action dated February 19, 2009.

(V) SUMMARY OF CLAIMED SUBJECT MATTER

The present invention, as claimed in claim 1 (from which claims 2-12 depend), relates to a fusion protein comprising i) an IgG Fc component, ii) an HIV envelope component, and iii) a C3d component.

Support for this aspect of the invention is found, for example, in claim 1 as originally filed, and at page 3, last full paragraph.

The present invention, as claimed in claim 13, relates to a complex comprising a fusion protein. The fusion protein comprises: i) an IgG Fc component, ii) an HIV envelope component, and iii) a C3d component. The HIV envelope component of the fusion protein is activated so that intermediate conformations of conserved neutralization epitopes of the HIV envelope component are exposed.

Support for this aspect of the invention is found, for example, in claims 1 and 13 as originally filed, and at page 3, last full paragraph, and at page 6, first full paragraph.

The present invention, as claimed in claim 14 (from which claims 15-17 depend), relates to a complex comprising a fusion protein. The fusion protein comprises: i) an IgG Fc component, ii) an HIV envelope component, and iii) a C3d component. The HIV envelope component is bound to a ligand that upregulates at least one of a CD4 binding site and a CCR5 binding site of the HIV envelope component.

Support for this aspect of the invention is found, for example, in claims 1 and 14 as originally filed.

(VI) GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The following grounds of rejection are presented for review:

Whether claims 1-12 would have been obvious under 35 USC 103(a) over Ross et al in view of Shearer et al, as evidenced by Rizzuto et al.

Whether claims 13, 14, 16 and 17 would have been obvious under 35 USC 103(a) over Ross et al in view of Shearer et al and DeVico, as evidenced by Rizzuto et al.

Whether claims 13-15 would have been obvious under 35 USC 103(a) over Ross et al in view of Shearer et al and Wyatt, as evidenced by Rizzuto et al.

(VII) ARGUMENT

REJECTION OF CLAIMS 1-12 UNDER 35 USC 103(a) AS OBVIOUS OVER ROSS ET AL IN VIEW OF SHEARER ET AL AS EVIDENCED BY RIZZUTO ET AL.

Claims 1-12 would not have been obvious over the combination upon which the Examiner relies and reversal is requested for the reasons that follow.

Ross et al relates to DNA vaccination with gp120-C3d fusion proteins. Ross et al report enhanced antibody titers and avidity maturation of antibodies to Env but poor titers of neutralizing antibody in vaccinated mice.

As the Examiner acknowledges, Ross et al is devoid of any teaching as regards a fusion protein comprising IgG Fc. The Examiner relies on Shearer et al to cure that deficiency.

Shearer et al relates to vertical transmission of HIV-1 and reports the results of a study designed to determine whether intraveneously administered rCD4-IgG crosses the human placenta and whether it can be detected in human neonates. The study was not designed to address the question of efficacy of the rCD4-IgG fusion in blocking vertical HIV-1 transmission. The results appear to demonstrate that the bifunctional molecule can be transported across the placenta. No significant accumulation of rCD4-IgG was observed in an infant born to a mother who received multiple injections of rCD4-IgG.

In rejecting the claims as obvious, the Examiner contends that it would have been obvious to add the human IgG Fc component to the N- or C-terminus of the gp120-C3d fusion protein of Ross et al for the purpose of increasing the serum half life of gp120-C3d

and that there would have been a reasonable expectation of success because Shearer et al suggests that human IgG Fc prolongs the serum half life of the gp120 binding domain of CD4. These assertions do not constitute the type of reasoning required to support the contention that the combination of references would have led an artisan to the claimed invention.

Rejections under 35 USC 103 must rest on a factual basis with the facts being interpreted without hindsight reconstruction of the invention from the cited art (see *In re Warner*, 379 F2d 1011, 1017 (CCPA 1967), *cert denied* 389 U.S. 1057 (1968)). The Examiner's basis for rejection here falls short of identifying a rationale that would have led one skilled in the art to combine features from each of the references in a way that would have resulted in the claimed product (see *KSR Int'l Co. v. Teleflex, Inc.*, 127 S.Ct. 1727, 1741 (2007).)

Stated otherwise, nothing in the references upon which the Examiner relies would have suggested their combination. Indeed, the Examiner does not contend otherwise. Rather, the Examiner merely points out that Shearer et al suggests the use of IgG Fc to prolong the serum have life of the gp120 binding domain of CD4. Nothing in Ross et al and/or Shearer et al would have suggested a fusion protein comprising IgG Fc, gp120 and C3d, nor would the references have provided any basis for a reasonable expectation of generating a successful product.

In summary, it is only with the present invention in mind that one would have been motivated to combine the teachings of Ross et al and Shearer et al. It is now well

established that such hindsight-based reasoning is improper. Reversal of the rejection is requested.

REJECTION OF CLAIMS 13, 14, 16 AND 17 UNDER 35 USC 103(a) AS OBVIOUS OVER ROSS ET AL IN VIEW OF SHEARER ET AL AND DEVICO ET AL, AS EVIDENCED BY RIZZUTO ET AL.

Claims 13, 14, 16 and 17 would not have been obvious over the combination upon which the Examiner relies and reversal is requested for the reasons that follow.

Claim 13 relates to a complex comprising the fusion protein of claim 1 wherein the HIV envelope component thereof is activated so that intermediate conformations of conserved neutralization epitopes are exposed. Claim 14, from which 16 and 17 depend, also relates to a complex comprising the fusion protein of claim 1. In claim 14, the HIV envelope component is bound to a ligand that upregulates at least one of a CD4 binding site and a CCR5 binding site of the envelope.

Ross et al relates to DNA vaccination with a gp120-C3d fusion and Shearer et al relates to the use of rCD4-IgG as a drug in blocking vertical transmission of HIV-1. As pointed out above, it is only with the present invention in mind that these documents would have been combined.

The Examiner acknowledges that neither Ross et al nor Shearer et al teaches activation of HIV envelope as required in claim 13 or binding of a ligand to envelope as required in claim 14. The Examiner looks to De Vico et al to cure these failing.

De Vico et al relates to a gp120-CD4 complex and reports that "the covalently bonded CD4-gp120 complexes are useful for raising neutralizing antibodies against various isolates of HIV-1 and against HIV-2."

Nothing in De Vico et al would have motivated an artisan to combine the teachings thereof with those of Ross et al (relating to DNA vaccination) and Shearer et al (relating to a vertical transmission blocking agent). Further, nothing in the combination upon which the Examiner relies in rejecting claims 13, 14, 16 and 17 would have provided basis for expecting success if all of the components had been assembled as claimed. Indeed, the Examiner does not indicate otherwise but, rather, the Examiner comments only on the combination of Shearer et al and Ross et al and, separately, on the combination of Ross et al and De Vico et al.

Reversal is requested.

REJECTION OF CLAIMS 13-15 UNDER 35 USC 103(a) AS OBVIOUS OVER ROSS ET AL IN VIEW OF SHEARER ET AL AND WYATT AS EVIDENCED BY RIZZUTO ET AL.

Claims 13-15 would not have been obvious over the combination upon which the Examiner relies and reversal is requested for the reasons that follow.

The failings of Ross et al and Shearer et al are detailed above.

The Examiner acknowledges that neither Ross et al nor Shearer et al teaches a ligand-bound HIV Env. The Examiner looks to Wyatt et al to cure that failing.

Wyatt et al relates to a complex comprising HIV gp120 bound to a monoclonal antibody.

Nothing in Wyatt et al would have motivated an artisan to combine the teachings thereof with those of Ross et al (relating to DNA vaccination) and Shearer et al (relating to a vertical transmission blocking agent). Further, nothing in the combination upon which the Examiner relies in rejecting claims 13-15 would have provided basis for expecting success if all of the components had been assembled as claimed. Indeed, the Examiner does not indicate otherwise but, rather, the Examiner comments only on the combination of Shearer et al and Ross et al and, separately, the combination of Ross et al and Wyatt et al.

Reversal of the rejection is requested.

CONCLUSION

In conclusion, it is believed that the application is in clear condition for allowance; therefore, early reversal of the Final Rejection and passage of the subject application to issue are earnestly solicited.

Respectfully submitted,

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(VIII) CLAIMS APPENDIX

1. A fusion protein comprising:

i) an IgG Fc component,

ii) an HIV envelope component, and

iii) a C3d component.

2. The protein according to claim 1 wherein said IgG Fc component is present in said fusion protein N-terminal to said HIV envelope component.

3. The protein according to claim 1 wherein said HIV envelope component is present in said fusion protein N-terminal to said C3d component.

4. The protein according to claim 1 wherein said IgG Fc component is present in said fusion protein N-terminal to said HIV envelope component and said HIV envelope component is present in said fusion protein N-terminal to said C3d component.

5. The protein according to claim 1 wherein said protein further comprises at least one intervening sequence between at least 2 of said components.

6. The protein according to claim 1 wherein said IgG Fc component is a human IgG Fc component.

7. The protein according to claim 1 wherein said C3d component is a human C3d.

8. The protein according to claim 1 wherein said C3d component targets said fusion protein to antigen presenting cells that express CD21 and thereby promotes antigen presentation.

9. The protein according to claim 1 wherein said HIV envelope component is HIV-1 gp120, gp140, gp160, gp41, or immunogenic portion of gp120 or gp41.

10. The protein according to claim 1 wherein said HIV envelope component comprises residues of the V3 domain of gp120 and includes a B cell neutralizing antibody epitope.

11. An immunogenic composition comprising at least one of said fusion proteins according to claim 1.

12. The composition according to claim 11 wherein said composition further comprises a carrier.

13. A complex comprising a fusion protein, said fusion protein comprising:

i) an IgG Fc component,

ii) an HIV envelope component, and

iii) a C3d component

wherein said HIV envelope component of said fusion protein is activated so that intermediate conformations of conserved neutralization epitopes of said HIV envelope component are exposed.

14. A complex comprising a fusion protein, said fusion protein comprising:

i) an IgG Fc component,

ii) an HIV envelope component, and

iii) a C3d component,

wherein said HIV envelope component is bound to a ligand that upregulates at least one of a CD4 binding site and a CCR5 binding site of said HIV envelope component.

15. The complex according to claim 14 wherein said ligand is an antibody, or Fab_2 or Fab fragment thereof.

16. The complex according to claim 14 wherein said ligand binds to a CCR5 binding site of said HIV envelope component and upregulates a CD4 binding site of said HIV envelope component.

17. The complex according to claim 16 wherein said ligand upregulates a CCR5 and a CD4 binding site on said HIV envelope component.

(IX) EVIDENCE APPENDIX

(NONE)

(X) RELATED PROCEEDINGS APPENDIX

(NONE)